

MARMITE

(YEAST EXTRACT)

IN MEDICINE AND
DIETETICS



=====with special reference to=====

Vitamin B Complex

Vitamin Potency

Beri-beri

Macrocytic Anaemias

Polyneuritis

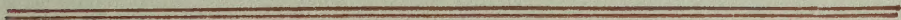
Tropical Medicine

Pellagra

Restricted Diets

Paediatrics

Pregnancy



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MARMITE

and

THE VITAMIN B COMPLEX

Nutrition and Health

The urgent need for the education of the community in the proper choice of food, in order to secure a better standard of health, is a subject which is engaging widespread attention. That the new knowledge of nutrition is of the utmost importance is stressed by the Ministry of Health (1938) and by those responsible for organising the National Health Campaign. The Ministry of Health's Advisory Committee on Nutrition (1937) emphasises the special need for the adequate provision in the diet of protective foods, including particularly those of high mineral and vitamin content. It is stated that "*various mineral elements and vitamins play roles as essential in the economy of the body as those played by the proteins, fats and carbohydrates.*"

Modern diets are frequently lacking in vitamin-containing foodstuffs, and many clinicians and research workers find that there is a particular tendency to deficiency of the vitamins of the B group. The value of Marmite as a rich source of all the known factors of the vitamin B complex is well appreciated, and there is ample proof of its efficacy. This autolysed yeast extract is being prescribed increasingly at home and abroad in preventive and curative medicine; it is ordered extensively in private practice and in hospitals, schools, welfare centres and clinics.

A few years ago only two vitamins of the B group were recognised. These were known as B₁, the anti-neuritic or anti-beri-beri factor, and B₂, the pellagra-preventing factor. Now, however, the vitamin B complex is known to comprise at least six components.

The Vitamin B Complex

A deficiency of vitamin B₁ (aneurin) is related to certain disorders of the alimentary, cardiovascular and nervous systems, and to faulty carbohydrate metabolism. The role of vitamin B₁ in carbohydrate metabolism has been worked out by Peters (1936; 1938), who has demonstrated that the presence of this factor is essential for the breakdown of the intermediary metabolite, pyruvic acid.

Vitamin B₁

Various estimates of the daily requirement of a normal healthy individual have been made. A minimum of 300 International Units per day has been specified in the Bulletin of the Health Organisation of the League of Nations (1938), but many authorities maintain that higher intakes are indicated, 700-1,000 International Units per day being a more desirable figure. In pregnancy there is an increased demand for vitamin B₁, and three times the normal requirement is advised.

Vitamin B₂ has proved to be composite and to consist of at least five entities. Of these only lactoflavin (riboflavin) and nicotinic acid have been clearly identified. Lactoflavin is now described as vitamin B₂. Although its exact relation to human nutrition has not been determined, this factor is deemed important in cell oxidation. Nicotinic acid is considered to be either a precursor of the pellagra-preventing factor or else the actual P.P. factor itself. It has been suggested that certain types of anaemia are connected with a deficiency of some part of the vitamin B₂ complex, possibly the fraction known as vitamin B₆.

Vitamin B₂ Complex

Vitamin Potency

Marmite contains all the known vitamins of the B complex, and its use in the treatment of diseases due to deficiency of these factors is well established. In order to be able to express the B₁ potency of samples of Marmite in terms of the International Unit, several batches have been tested by a recognised authority using different samples of Marmite for each experiment.

Marmite is not standardised, but these estimations have shown the samples under investigation to contain 840 International Units of vitamin B₁ per ounce, or 30 International Units per gramme. The figures quoted above have been obtained by testing different samples of fresh material. Pigeons have been used as experimental animals and the technique has been that described by Coward, Burn, Ling and Morgan (1933).

In view of the known tendency of some vitamin preparations to lose in potency on storage, samples of Marmite taken from one particular batch have been examined at various intervals of time. These preliminary experiments indicate that the B₁ potency diminishes to a certain extent during the first 15 months. Thereafter no appreciable decrease has been observed when testing the same material after further periods of 6, 12 and 18 months. For most purposes this diminution in the B₁ content of Marmite may be of little importance, but the research worker who is seeking precise information upon some technical problem should take it into consideration. Experimental evidence suggests that the activity of the other members of the B complex is unaffected by storage.

No International Standards exist for the other vitamins of the B group, but attempts have been made to estimate both lactoflavin and nicotinic acid. Kuhn and others (1934) have reported that Marmite contains 3.30 mg. lactoflavin per 100 g. and this confirms the opinion formed from feeding and other experiments to the effect that Marmite is rich in vitamin B₂. The precise estimation of nicotinic acid is still at the

experimental stage, but Knight (1937) has demonstrated the presence of this substance in yeast extract (Marmite), and dried brewers' yeast has been shown to contain 62·5 mgm. per 100 g. nicotinic acid (Swaminathan 1938).

Beri-beri is held to be caused by a deficiency of vitamin B₁—a deficiency which is known to give rise to faulty carbohydrate metabolism (Peters 1938). In support of this theory Platt (1938) reports that he has observed the presence of increased amounts of pyruvic acid in the blood of patients with uncomplicated fulminating beri-beri. He affirms that vitamin B₁ usually provides an effective cure.

Beri-Beri

Marmite is prescribed systematically with beneficial results in Malaya, Java, India, Burma, China, Egypt and other territories where beri-beri is prevalent. Recording their findings in cases of beri-beri in China, Platt and Lu (1936) state: "*The patient had approximately 750 international units of vitamin B₁, mainly as Marmite. The oedema, cyanosis, and distressing dyspnoea and the sensation of epigastric oppression gradually subsided during the first 5-6 days. . . . He was discharged at the end of one month apparently quite well.*" Similar success obtained with Marmite therapy in cases of beri-beri is reported from Egypt by Day (1936), who observes: "*Marmite was begun and within a week the oedema, ascites and enlargement of the liver had disappeared.*"

Several consignments of Marmite have been sent to China where the incidence of beri-beri among the refugees is high. The Acting Director of the Henry Lester Institute of Medical Research, Shanghai (1938), writes: "*The supplies of Marmite sent out to China have been of great value in the treatment of beri-beri. The high content of vitamin B in Marmite together with the other extractives from yeast, provided a valuable remedy for the cases of multiple dietary deficiency. The severe cases were given one ounce a day and the milder cases half an ounce,*

producing the expected result of a complete cure of the beri-beri cases of the dry type."

Polyneuritis It is acknowledged that the polyneuritis of beri-beri is associated with deficiency of vitamin B₁, and that it responds to Marmite therapy. Other forms of polyneuritis, especially those connected with alcoholism, pregnancy and gastro-intestinal lesions, also appear to be related to avitaminosis B. Strauss (1935) declares that "*'alcoholic' polyneuritis may be regarded as similar to the polyneuritis of beri-beri and treated accordingly.*" He employs Marmite* treatment with success in this condition. Goodhart and Jolliffe (1938) conclude that "*vitamin B deficiency is the primary cause of the polyneuritis of the alcohol addict.*" They report success in a case "*treated as an out-patient with a diet rich in vitamin B supplemented by three teaspoonfuls of Vegex* daily.*" Price (1938) also considers that insufficient intake of vitamin B may be a responsible factor and recommends a good diet, supplemented with Marmite.

Laurent and Sinclair (1938) report a case of peripheral neuritis associated with pyloric stenosis which is "*of unusual interest because of the clear association of the symptoms with deficiency of vitamin B₁.*" They state that the patient "*was advised to take Marmite, 2 drachms daily. . . . He made a gradual improvement and returned to work.*" Several months later he was reported to be feeling well, and "*still takes Marmite, 8 oz. per week.*" Sargant and Fraser (1938) consider that "*vitamin deficiency plays an important part in the production of peripheral neuritis and the toxic cerebral disorders of the Korsakow type, especially those due to pregnancy and alcohol,*" and they recommend that "*a yeast preparation, such as Marmite, one teaspoonful t.d.s., should be prescribed.*"

* Marmite is known as Vegex in the U.S.A.

Clinical resemblances between polyneuritis occurring in pregnancy and beri-beri have been observed by Theobald (1936), and the frequent association of polyneuritis with gastric and intestinal symptoms is well known. In discussing this subject, Ungley (1938) remarks that "*on the whole the evidence available justifies the belief that polyneuritis associated with alcoholism, pregnancy, and gastro-intestinal lesions is due, in some cases at least, to nutritional deficiency. Aetiological factors are low intake, poor assimilation, and increased utilisation of vitamin B₁.*" Experience has shown that Marmite, which is rich in all the vitamins of the B group, is successful both in the treatment and prevention of these conditions which arise from such a nutritional deficiency. The spectacular response to Marmite observed in cases of retrobulbar neuritis is described on p. 8.

Many common disturbances of the alimentary system are ascribed to avitaminosis B. McCarrison (1936a) stresses the fundamental relation of vitamin B deficiency to gastro-intestinal dysfunction. Not only B₁ but also the B₂ complex appears to be required for the functional efficiency of the tract, shortage of B₁ being associated with impairment of secretory and motor functions, while lack of the B₂ factors is said to lead to degenerative and inflammatory conditions. Describing the prevalence and consequences of mild degrees of vitamin deprivation, McCarrison (1936b) states: "*So, too, with vitamin B: poor appetite, some digestive disturbance, nervousness, feeble action of the heart, lack of vigour and fatigue may be evidences of its inadequate supply, where no signs of beri-beri exist.*" He emphasises the point that "*it is the lesser degrees of vitamin-deficiency, and the less obvious manifestations of such deficiency that are of importance in Western countries.*"

Gastro-Intestinal Disturbances

In the treatment of gastric and duodenal ulcers Marmite is often prescribed. Witts (1938) remarks that "*the rise of peptic ulcer as a cause of illness and death in Western Europe can be fairly closely correlated with a*

fall in the intake of vitamin B." He includes Marmite in the diet prescribed for the medical treatment of these ulcers. Outlining the dietetic treatment of gastroduodenal haemorrhage, Witts (1937) states: "*Marmite is given at least once a day for the vitamin B complex.*"

Pellagra

For some years pellagra has been considered as a nutritional disease associated with a deficiency of some fraction of the vitamin B complex. There is ample proof that the disease can be both prevented and cured by the administration of Marmite.

Recently attention has been focused upon nicotinic acid, and its identity with the pellagra-preventing (P.P.) factor has been postulated. It is of interest to note that Knight (1937) has demonstrated the presence of nicotinic acid in yeast extract, and that Marmite was the yeast extract used in this research. Successful clinical trials with nicotinic acid in human pellagra have already been reported.

Moore (1937) has commented on "*the dramatic effect of Marmite on the skin lesions*" of pellagrous conditions. After describing the prevalence of pellagrous symptoms among school children in Nigeria, he remarks that "*the disease itself is curable with Marmite alone . . .*" thus confirming his earlier observations. Moore reports that "*over 200 selected patients were treated for a period up to 10 months with yeast or Marmite alone—the majority with Marmite owing to its more stable properties. All skin conditions cleared up rapidly, and the visual response was entirely in keeping with results formerly obtained.*" In these cases retrobulbar neuritis and partial optic atrophy accompanied the pellagrous skin lesions. This work has been further confirmed by more recent investigations (1938), in which the same observer has obtained equally good results with Marmite after eliminating the B₁ factor by autoclaving.

Similar conditions, and successful results obtained with Marmite, have been recorded by Landor and Pallister

in Malaya (1935). Referring to their work, Stannus (1936) reports that "*50 early cases were 'cured' after 15 gm. Marmite daily for one month, 20 relapsed within a month of ceasing to take it!*"

Confirmatory evidence of the value of Marmite in pellagrous lesions comes from West Africa (Dodds 1937), Egypt (1934), and India (Mody 1935). In publishing details of the recovery of a pellagra patient, Gupta (1935) remarks that "*the most important item in her treatment was the supply of vitamin B₂; she was given Marmite one teaspoonful thrice daily and improved steadily.*" Trowell (1937) has described the occurrence of pellagra in African children. The symptoms, although not identical with those found in adults, were cured with Marmite. To these patients, aged 6 months to 4 years, "*Marmite was given in doses of a teaspoonful a day for every year of age.*"

Certain skin conditions respond to Marmite, especially those associated with constipation and defective diets. Cases of furunculosis, in particular, have shown marked improvement when Marmite has been added to the diet. The value of Marmite in pellagrous skin lesions has already been mentioned. Similar lesions have been observed in certain anaemias which "*responded as dramatically as the blood picture to the administration of Marmite*" (Vaughan and Hunter 1932).

Skin Diseases

Experimental evidence indicates that susceptibility to leprosy infection may be increased by vitamin B deficiency, and analogies between beri-beri, pellagra and leprosy have been suggested. Brown (1935), working in Nigeria, has reported favourably on the use of Marmite in leprosy—a disease endemic where diets are unsatisfactory and avitaminosis common. The following case report is typical:—"Case 59. Complained of indigestion, irritation in the skin, and oedema. These disappeared with Marmite, and he was very emphatic about the improvement."

Prevention of Infection

The administration of Marmite appears to stimulate resistance to infection, and is therefore advocated in influenza epidemics and when other infectious diseases are prevalent. The value of Marmite in this respect may be connected with the fact that the vitamin B complex "*contributes so markedly to the prevention of microbic invasion of the body*" (McCarrison 1936b). It is now generally agreed that "*deficiency of the vitamin-B complex may be related to increased susceptibility to certain kinds of infection*" (Cowell 1937).

Restricted Diets

In prescribing restricted diets particular care is required to guard against vitamin deficiency, especially a deficiency of the vitamin B complex. It is largely for this reason that Marmite is ordered for inclusion in most invalid diets, and is listed on the diet sheets of many hospitals. It not only compensates for lack of vitamin B but also provides an agreeable flavouring and stimulates the appetite. In recommending suitable sources of vitamins, Willcox (1938) mentions that "*vitamin B may be given as Marmite . . .*" Its special value in anorexia is widely appreciated.

Marmite is particularly indicated for diabetics and for those on a reducing diet, as it contains no carbohydrates or fats and only a negligible quantity of true protein; it need not, therefore, be included in the dietetic calculations. Archer (1938), referring to diabetic diets for children, mentions that "*there is little likelihood of vitamin or mineral salts deficiency except in the case of vitamin B. . . . Marmite is a very convenient form to give.*"

The connection between colitis and vitamin B deficiency has been discussed by Hare (1935) who advises the administration of Marmite to colitis patients. This practice is also advocated by Graham (1935), Patterson (1936), and also by T. P. Williams (1936) who says: "*Medicinal treatment is not always required provided that we see that the vitamin requirements are satisfied, especially for the 'B' complex.*"

Many other conditions occur in which dietary restriction is essential and in which Marmite is of considerable value. It is useful in certain of the diets ordered for gastric and duodenal ulcer patients. It is a desirable constituent of a ketogenic diet, but may also be given with advantage when fat is prohibited. It has a special use in coeliac disease, as it helps to combat the associated anaemia, and also provides vitamin B. Morris (1938) suggests that in coeliac disease "*vitamin B may be supplied as Marmite.*" Wilkinson (1936) states that in cases of nutritional hypochromic anaemia "*the addition of one teaspoonful of Marmite daily . . . is of great value,*" as there is a tendency to vitamin B₂ deficiency.

In recommending a suitable diet for rheumatoid arthritis, Buckley (1938) stresses the need to "*ensure an ample supply of vitamins in due proportion*" and he includes Marmite in the dietary scheme.

The health of the child is regarded as of such fundamental importance that the Mixed Committee on the Problem of Nutrition, appointed by the League of Nations, refer to it in their Interim Report (1936) as "*the kernel of the problem.*" Many paediatricians consider that a large number of children to-day receive sub-optimal amounts of vitamin B, and that irreparable damage is often thus inflicted in childhood. Reinforcing the diets of children with extra supplies of vitamin B₁ has resulted in improved health and increase in weight and height. **Paediatrics**

Referring to the vitamin requirements of children, Friend (1936) says: "*probably the B group is that most likely to be short in school diets.*" Pritchard (1935) states that "*the vitamin most commonly provided in insufficient quantity for toddlers is vitamin B.*" He considers (1938) that "*it is advisable to be on the safe side and give all children supplementary supplies of vitamin B*" and recommends the administration of Marmite, remarking that it "*appears to be particularly rich in the B₂ factor.*" The value of Marmite in

paediatric practice is also appreciated by Parsons and Barling (1933), and by Paterson (1937).

In connection with recent outbreaks of poliomyelitis, the suggested use of vitamin B therapy, to prevent paralytic involvement, is of interest. McCormick (1938) states: "*With the established anti-paralytic effect of vitamin B in beri-beri it would seem that this pioneer in the vitamin field should offer the most hope of protective value in poliomyelitis.*" Marmite is being ordered by physicians who are testing this theory.

In the Medical Research Council Report (1932) on vitamins, the view is expressed that, as a safeguard, all children should be given "*Marmite for vitamin B complex—a small quantity daily.*" Children can often be tempted to eat Marmite sandwiches even when they refuse other food. It is therefore particularly useful for administration to debilitated children with anorexia. Marmite is also especially indicated in malnutrition, anaemia and wasting disease.

Pregnancy and Lactation

The attention of the medical profession, the Government and the general public has recently been directed to the success of the nutrition scheme inaugurated by the National Birthday Trust Fund, whereby additional foods have been distributed to groups of necessitous expectant mothers in the depressed areas. Among those women receiving the food supplements a most striking fall in the maternal death rate has been observed, and also increased well-being of mothers and infants.

The experiment was started in the Rhondda Valley in December, 1934. Medical experts recommended the inclusion of Marmite in the short list of selected food-stuffs, and there is reason to think that the extra supply of the vitamin B complex thus provided may have played an important part in the prevention of disorders complicating pregnancy.

M'Gonigle (1937) says that "*those who have followed the interesting experiment carried out in South Wales under the direction of Lady (Rhys) Williams, in which the diet of expectant mothers has been very materially increased in regard to protein and the B group of vitamins among other supplements such as milk, must have been impressed with the results. . . . If the results so far obtained during a relatively short time are continued it would appear as if the nutritional factor in maternal mortality is of the utmost importance and provides the key to the solution of a great social problem.*"

The drop in the puerperal death rate was so spectacular (from 11.29 in 1934 to 4.77 in 1935 per 1,000 total births) that in 1936-37 a grant was secured from the Commissioner for the Special Areas in order to extend the food distribution to other scheduled areas (Williams 1937). In 1937-38 a further grant was obtained so that groups of women in all the special areas of England and Wales could receive the extra foodstuffs (Williams 1938).

A report on the results, published in 1937, shows that among 10,384 women given the supplementary food the maternal death rate was 1.63 per 1,000 total births, whereas among 18,854 not given the food the death rate was as high as 6.15.

Balfour (1938), giving details of the investigations of the research committee instituted in 1937 by the Joint Council of Midwifery to administer the nutrition scheme on a scientific basis, states: "*Speaking generally, the Birthday Trust provides for each woman 3 lb. of milky foods and half a pound of Marmite per month for three months previous to the confinement. . . .*" It has been recorded (Brit. med. J., 1938b) that "*The Marmite . . . was rich in the vitamin B complex, which was a neuro-muscular stimulant. . . . Another point was that Marmite had a very important haemopoietic action which was not understood and was probably not associated with any of the vitamin B constituents at present recognised.*"

In response to a request made in Parliament in May, 1938, the Minister of Health circulated a table showing results obtained for the last six months of 1937. The total puerperal death rate in the groups not receiving special food was 3.54 per 1,000 total births, but that in the group receiving the food was only 0.45 (Brit. med. J., 1938a).

As an outcome of these and other investigations, many doctors urge that Marmite should be added to the diet of all women as a routine measure during both pre-natal and post-natal periods. According to McIlroy (1937), "*the diseases of pregnancy . . . should be classified as deficiency diseases.*" She remarks (1936) that on account of its vitamin content and its anti-anaemic properties, "*Marmite—a preparation of autolysed yeast—should be given in soups or as sandwiches with wholemeal bread and butter.*"

MARMITE

as

ANTI-ANAEMIC AGENT

In 1931 Wills discovered that Marmite exerted a specific curative action in cases of tropical macrocytic anaemia. It was noted by the Medical Research Council (1932) that "*this investigator observed dramatic improvement and cure when such cases were treated with a yeast extract (Marmite) rich in vitamins B₁ and B₂.*" The fact that this form of anaemia "*is invariably cured by Marmite*" (Vaughan 1936) has now become well established.

The original work on tropical macrocytic anaemia, which led to the use of Marmite as a haemopoietic agent, was carried out in India, where this anaemia is a serious menace. It is often associated with malaria and hook-worm disease and has a particularly high incidence among pregnant women. Tropical macrocytic anaemia is held to be a deficiency disease due to the absence of some essential haemopoietic principle in the diet. It occurs not only in India but also in other territories—including particularly China, Malaya and the West Coast of Africa—where faulty nutrition is common. Recently this form of anaemia has also been recognised in non-tropical countries (Fairley and others 1938 Groen and Snapper 1937).

Tropical Macrocytic Anaemia

There is abundant evidence proving that this anaemia responds to Marmite therapy. Wills (1933a) states: "*further trials have confirmed my previous findings as to the curative action of this preparation . . . in the majority of cases, even those with counts as low as one million, the response to Marmite in adequate doses is so rapid that the more expensive treatment is rarely necessary.*" In 1934 the same investigator emphasised the importance of prevention and recommended that "*as a prophylactic measure, in areas where the condition is endemic, education and public health policy should encourage . . . the*

use of some autolysed yeast product such as Marmite." Recently Wills (1937; 1938) has re-affirmed that in this form of anaemia Marmite is curative by itself.

The curative effect of Marmite in tropical macrocytic anaemia in India has also been described by Napier (1936). Whereas most of the patients treated by Wills were pregnant women, Napier's patients were all either men or non-pregnant women. In the summary of his paper, Napier states: "*Among the cases of anaemia admitted to the Hospital for Tropical Diseases in Calcutta during the last year, there were 11 cases of macrocytic anaemia that responded to treatment with Marmite; 4 of these patients were non-pregnant women and 7 were men.*" He is so convinced of the activity of Marmite that he has "*established a Marmite 'tradition' in the hospital amongst patients and nurses.*" In a more recent paper, Napier and collaborators (1938) again refer to the efficacy of Marmite in this connection.

McRobert (1938), working in Madras, also reports success with Marmite treatment when applied in cases of macrocytic anaemia in male Indian coolies. He says: "*I have never found in India a case of anaemia which failed to respond to massive doses of Marmite and which subsequently responded to the administration of liver.*"

When associated with pregnancy, tropical macrocytic anaemia usually occurs in a very severe form, and maternal mortality is high unless effective treatment is adopted. Workers in Bombay, Calcutta, Malaya and elsewhere have published convincing accounts of the value of Marmite in such cases. Green-Armytage (1932), describing this anaemia, which is a grave social problem in India, records "*excellent results with Marmite given in 2 teaspoonful doses twice a day either in cold water or in soup. Marmite is very cheap and is uniformly more popular with patients than is liver, being of vegetable origin.*" In later reports Green-Armytage (1934; 1935) remarks that, whereas the tropical macrocytic anaemias of pregnancy were hitherto "*often treated by*

liver or stomach preparations, and there was no reticulocyte response, now . . . we can practically assure recovery by giving Marmite, $\frac{1}{2}$ to $\frac{3}{4}$ oz. a day." He describes Marmite therapy as "*almost a specific method of treatment.*"

The specific use of Marmite in a similar form of anaemia in British Guiana is described by Giglioli (1934; 1937). The anaemia is apparently not identical with that found in India, but it also affects pregnant women particularly, though not exclusively. Cook (1935) comments upon the high mortality from tropical macrocytic anaemia among pregnant women in Uganda, where the disease has been confused with ankylostomiasis. He states that "*liver diet and Marmite seem the best remedies.*"

The striking results observed when Marmite was used therapeutically in tropical macrocytic anaemia led to its use in other types of macrocytic anaemia. Vaughan (1933) recommends the trial of Marmite for two weeks wherever applicable in hyperchromic anaemias, "*since it is far less expensive than liver or stomach.*"

Anaemia of Sprue

The anaemia associated with sprue is believed to be due to failure in the absorption of the liver principle curative in pernicious anaemia. It seems, however, that another factor, present in Marmite but not yet identified, may be involved (Wills and Evans 1938). Reports have been published which demonstrate the value of Marmite therapy in sprue. Comrie (1937) finds that "*many patients are greatly benefited by the oral administration of Marmite,*" and Castle, Rhoads, Lawson and Payne (1935) record that in certain cases of sprue "*the effect of 12 Gm. of Vegex* was greater than the effect of liver extract derived from 300 Gm. of liver.*" The inclusion of Marmite in the special diets prescribed for patients with sprue has been recommended by Graham (1935), Cooke (1938), Rogers (1932) and Castle and Rhoads (1932).

* Marmite is known as Vegex in the U.S.A.

Marmite therapy in sprue is a matter of routine in the Army Medical Service, as well as in general hospitals and in private practice. Its use in sprue is noted in the Army publication, "Memoranda on Medical Diseases in Tropical and Sub-tropical Areas, 1930" (H.M. Stationery Office), and also in "Recent Progress in Medicine and Surgery, 1919-1933."

Anaemia of Coeliac Disease

The effect of Marmite on the macrocytic anaemia associated with coeliac disease has been studied by Vaughan and Hunter (1932), who reported that "*the response of the anaemia to Marmite was as dramatic as that obtained by the administration of liver extract in the treatment of Addisonian pernicious anaemia,*" and these findings were later substantiated (Bennett, Hunter and Vaughan 1932; Vaughan 1936). Parsons and Smallwood (1935) note that "*rapid cure of some instances in adults suffering from coeliac disease has followed the administration of large doses of Marmite.*"

It has been observed that the macrocytic anaemia of coeliac disease may often be prevented if Marmite be given regularly, a custom which is commended by Parsons and Barling (1933), and also by Paterson and Forest Smith (1935). The administration of Marmite in coeliac disease serves a dual purpose, since vitamin B₁ therapy is indicated in addition to anti-anaemic treatment. Marmite provides the B₁ factor and a haemopoietic principle. Recently Parsons (1938) has drawn attention to the fact that carbohydrate, as well as fat absorption, is poor in coeliac disease, and states that "*vitamin B₁ (as Marmite) was also now given as a routine measure.*"

Pernicious Anaemia

The use of Marmite in the treatment of pernicious anaemia has been investigated by several haematologists. A paper published in 1932 by Goodall stimulated interest in this subject. He reported: "*Marmite in large doses is a satisfactory remedy for primary and relapse cases of pernicious anaemia of moderate severity. . . . I have treated all my 'maintenance' cases with Marmite.*"

Without exception, these have done well." In 1933, Wilkinson and Klein noted that several workers, including themselves, had "*obtained responses in cases of pernicious anaemia by the use of Marmite alone.*" Referring to pernicious anaemia, Vaughan (1936) states that "*certain patients respond to large doses of Marmite.*"

These positive results obtained with Marmite alone have been explained by assuming that gastric secretion was only partially impaired and the intrinsic factor, referred to below, not entirely absent. There is conclusive evidence of the efficacy of Marmite therapy in cases where the intrinsic factor is administered simultaneously as well as in the less severe cases where complete absence of the intrinsic factor probably does not obtain.

Marmite given alone, or auxiliary to other treatment, is welcomed by pernicious anaemia patients, as it is palatable and inexpensive—two important considerations in prescribing a treatment which must be continued indefinitely. It is recommended particularly for maintenance cases.

In 1932 Strauss and Castle postulated the theory that normal haemopoiesis is dependent upon the interaction of an intrinsic factor present in healthy human gastric juice, and an extrinsic factor supplied by certain foods. According to this hypothesis, hyperchromic macrocytic anaemias are due to a deficiency of this product of reaction—the deficiency being caused by lack of either the intrinsic or the extrinsic factor, or by inability to utilise the fully-formed product.

Aetiology of Macrocytic Anaemias

Research on the aetiology of the anaemias centred round this idea for some time, and it has been submitted that some macrocytic anaemias may be cured simply by supplying sufficient extrinsic factor, whereas in other anaemias, notably in Addisonian pernicious anaemia, there is also a deficiency of intrinsic factor, and cure is only possible if the complete haemopoietic principle is supplied. As a result of recent work, however, Wills and others (1937 ; 1938) infer that the type of anaemia

formerly attributed solely to lack of extrinsic factor, and consequent failure in production of active haemopoietic principle, may be due to deficiency of a second haemopoietic factor. This new factor has not yet been identified, but there is reason to believe that it may be related to some fraction of the vitamin B₂ complex, although it is not lactoflavin or nicotinic acid.

Napier's experiments (1938) also suggest the existence of an independent active principle, other than the extrinsic factor, essential for normal haemopoiesis. He refers to it as the "*Marmite principle*," since it is present in Marmite.

The Extrinsic Factor

The nature of the extrinsic factor has been under discussion since 1932, when Strauss and Castle suggested that it was identical with the factor then known as vitamin B₂. This supposition was contested by Wills (1934), who conducted elaborate experiments which indicated that the haemopoietic factor present in Marmite was not one of the known B vitamins.

Miller and Rhoads (1934) also formed the opinion that the anti-anaemic factor found in Marmite* was not vitamin B₂. Ungley (1938), referring to earlier work (Ungley and James 1934), "*found that 'vitamin B₂ concentrates' prepared from yeast were relatively ineffective as a source of extrinsic factor, whereas a fraction of Marmite administered subsequently gave an excellent response.*" West (1935) agrees that the extrinsic factor and vitamin B₂ are separate entities, and observes that Marmite* contains the extrinsic factor.

Since the discovery that vitamin B₂ consists of more than one factor, further enquiry has been made into the nature of anti-anaemic substances. The identity of the extrinsic factor is still not clear, but there is evidence to show that it differs from lactoflavin, the fraction B₆, and nicotinic acid.

* Marmite is known as Vegex in the U.S.A.

The investigations which have established that Marmite possesses definite haemopoietic properties have been closely linked up with research on the aetiology of the macrocytic anaemias. The haemopoietic activity of Marmite was originally ascribed to its high content of Castle's extrinsic factor. Recently Wills and others (1937 ; 1938) have reported the existence of a second haemopoietic factor in Marmite. Although the nature of these factors is still obscure, it is clear that Marmite is a rich source of both the extrinsic factor and the active principle described by Wills.

The Haemopoietic Activity of Marmite

The fact remains that the administration of Marmite in the treatment of certain types of anaemia is followed by dramatic results ; in cases of tropical macrocytic anaemia Marmite therapy is regarded as a "*life-saving*" measure (Fairley 1935) ; it has been described as "*the treatment of choice*" (Gigliolo 1934).

Nutritional diseases are particularly common in tropical and sub-tropical countries, where the diets of the people are so often inadequate, and the prominent part played by deficiency of vitamin B₁ and the B₂ complex is attracting the notice of research workers and of government authorities. The special applicability of Marmite, whether used as a medicine or as a food, in India and other tropical countries depends not only on its proved medicinal properties, but also on the fact that it is purely vegetable in origin and may therefore be taken freely by all those who, for religious or other reasons, insist upon a strictly vegetarian diet. Another point of practical importance is that it is economical in use and is not affected by climatic conditions.

Marmite in Tropical Medicine

Marmite is prescribed prophylactically and therapeutically in many countries including India, Burma, Malaya, China, Java, Egypt and Africa, its specific use in tropical medicine being to combat beri-beri, pellagra and tropical macrocytic anaemia.

ADMINISTRATION AND DOSAGE

Marmite is easy to administer as it may be served in a variety of appetising ways. Frequently it is given as a clear soup, prepared by stirring a small teaspoonful of the extract into a cupful of hot water; a beaten egg may be added, or, when allowed, 1 or 2 teaspoonfuls of sherry. When made with hot milk it is usually popular, while iced Marmite is often appreciated. Marmite made into a paste with three times the quantity of butter forms an excellent sandwich filling, which may be spread on bread, toast, rusks or biscuits. Marmite may be incorporated in a variety of soups and savoury dishes.

For infants Marmite is added to the ordinary feeds, and for older children it is spread on rusks or served as broth.

When raw liver is prescribed in pernicious anaemia, physicians often advise that Marmite should be mixed with it to disguise the flavour and enhance the effect.

The administration of sufficient active material is of the utmost importance in the treatment of disease, and it is essential to administer an adequate quantity of Marmite in order to achieve success.

<i>Indication</i>				<i>Daily Dose</i>
Vitamin B Deficiency	..	..	..	$\frac{1}{2}$ to 2 ounces
Infants	..	..	..	$\frac{1}{2}$ to 2 drachms
Pregnancy	..	..	..	2 to 3 drachms
Tropical Macrocytic Anaemia			..	$\frac{1}{2}$ to 1 ounce
Anaemia of Coeliac Disease	..		..	3 drachms
Anaemia of Sprue	..	..	..	3 drachms
Pernicious Anaemia	..	..	..	$1\frac{1}{2}$ to 4 ounces

The above table is given as a rough indication of the amount of Marmite generally used in various conditions. It should be noted that a teaspoonful of Marmite is more than 1 drachm. In compiling this table from case reports it has not always been possible to ascertain whether the Marmite was weighed or measured from a spoon. The appropriate dose for each case is best found by trial.

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